DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/18/10 has been entered.

2. Claims 19-30 are pending.
Claims 21 and 22 stand withdrawn from further consideration by the examiner under 37CFR 1.142(b) as being drawn to a nonelected invention.

Since a prior art revealed no prior art on SEQ ID NO:5, the search has extended to include SEQ ID NO:1.

Claims 19, 20, 23-27 and 28-30 read on SEQ ID NO:1 as an amyloid peptide and palmitic acid as elected species are under consideration in the instant application.

3. Applicants' submission of IDS filed on 2/15/11 and 6/11/11 has been acknowledged.

4. The title of the invention is not descriptive. A new title that is required that is clearly indicative of the invention to which the claims are directed.

5. The following rejections remain.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 19, 20 and 23-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of enhancing antigenicity by administering supramolecular antigenic construct comprising an antigenic peptide set forth in SEQ ID NO:1-6 with a modification, does not reasonably provide enablement for methods to increase memory restoration and curiosity awakening comprising administering supramolecular antigenic constructs with GXXXGXXXGG or GXXXG peptide motifs or the use of supramolecular constructs to treat disorders comprising Alzheimer's diseases, multidrug resistance in cancer cells or prion diseases.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed.Cir.1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of the skilled in the art to practice the claimed invention.

The claimed is drawn to the method of improving pathological conditions (e.g. increased memory restoration and curiosity awakening) of Alzheimer's disease comprising administering a supramolecular constructs of any GXXXGXXXGG or GXXXG peptide motifs and the construct may be used in treating disorders comprising Alzheimer's disease, multidrug resistance in cancer cells or prion diseases. Wolf-Klein et al teaches that there is no medical treatment currently available to cure of stop the progression of Alzheimer's disease (Wolf-Klein et al., Am Journal of Hosp Palliat Care, 2007, 24(1):77-82, abstract, in particular, of record) despite of current pharmaceutical advances in delaying disease progression. Even though there are five FDA approved Alzheimer's drugs, they temporarily relieve some symptoms of the diseases. Further, Wolf-Klein et al. discloses that the length of survival has not changed despite new technology

and therapeutic approaches and the tolls of this incurable disease continue to increase (abstract, p. 77, 2nd col.)

Tagliavini et al. (Journal of Virology, 2003, vol. 77, no. 15, p. 8462-8469, of record) teach that there is no effective therapy for prion diseases including spongiform encephalopathy and Creutfeldt-Jacob diseases and some candidates are still being validated (abstract, discussion, in particular)

In addition, Applicants have not provided any *in vivo* working examples that the supramolecular constructs with GXXXGXXXGG or GXXXG peptide motifs can be used in treatment for multidrug resistance in cancer cells or prion diseases.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed supramolecular constructs in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Applicant's response and amendments to the claims filed on 8/18/10 have been fully considered but they were not persuasive.

Applicant has asserted that the present amendment reciting "enhancing antigenicity in a patient suffering from Alzheimer's disease" obviates the rejection.

Contrary to Applicant's assertion, the claimed invention is not limited to enhance the antigenicity but also recites improvement of pathological conditions of Alzheimer's diseases including memory restoration and curiosity awakening with any supramolecular antigenic constructs including GXXXGXXXGG or GXXXG peptide motifs. Further, claim 27 is drawn to treatment of Alzheimer's diseases and other prior diseases. As discussed above, Wolf-Klein et al teaches that there is no medical treatment currently available to cure or stop the progression of Alzheimer's disease (Wolf-Klein et al., Am Journal of Hosp Palliat Care, 2007, 24(1):77-82, abstract, in particular, of record) despite of current pharmaceutical advances in delaying disease progression. Even though there are five FDA approved Alzheimer's drugs, they temporarily relieve some symptoms of the diseases. Further, Wolf-Klein et al. discloses that the length of survival has not changed despite new technology and therapeutic approaches and the tolls of this incurable disease continue to increase (abstract, p. 77, 2nd col.). Moreover, the specification of the instant application in p. 3 acknowledges that the delaying and reversing the progression is largely unsuccessful. The specification of the instant application states:

> The management of AD consists of medication-based and non-medication based treatments. Treatments aimed at changing the underlying course of the diseases (delaying or reversing the progression) have so far been largely unsuccessful.

Further, claim 27 recites the intended use of the constructs in treatment for AD, multidrug resistance in cancer cells or prion diseases. For the reasons addressed previously, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed supramolecular constructs in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

8. Claims 19, 20 and 23-30 stand rejected under 35. U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of supramolecular antigenic constructs wherein the antigenic construct is a SEQ ID NOs:1-6 with a modification such as palmitoylation; however, Applicant is not in possession of any supramolecular antigenic constructs comprising any unspecified amyloid peptide motifs including GXXXG and GXXXGXXXGG or any fragments thereof.

The claims broadly encompass any peptides from any amyloid proteins in any lengths. The specification does not provide written description for such broad genus peptide encompassed by the claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The guidelines of the Examination of Patent Applications Under the 35 U.S.C. 112 § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e.., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying

characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Fri. January 5, 2001, see especially page 1106, column 3).

The antigenic peptide of the instant claims is drawn to any peptide that is obtained from any amyloid protein and some may have GXXXG and GXXXGXXXGG motifs. The specification of the instant application discloses some peptides (as in claim 25) that are derived from Aβ amyloid. However, the claimed peptide is not limited to Aβ amyloid but encompasses any amyloid proteins and the fragments thereof. It is noted that amyloid is defined as any complex protein that is deposited in tissues and shares selected laboratory features such as a change in the fluorescence intensity of certain aromatic dyes (Medicine Net definition, 8/8/04, of record) and there are number of other amyloids does not have any structural relationship with Aβ amyloid (wikipedia, 2009, p. 1-6, of record). Given that the broad range of peptides is claimed, it is apparent that the instant specification fails to disclose any species of peptides that are non Aβ amyloid. Thus, the failure of disclosure is not sufficiently representative of the broad genus of structurally different antigenic peptides other than Aβ amyloid sequences of claim 25.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant's arguments filed on 8/18/10 have been fully considered but they were not persuasive.

Applicant has asserted that the current amendment reciting "construct consisting an antigenic peptide consisting of the amino acid sequence of β amyloid or an active fragment thereof" provides sufficient written description and obviates the rejection.

Contrary to Applicant's assertion, the claimed peptide is not limited to β amyloid or fragments thereof but includes any antigenic polypeptide that encompasses the fragment of β amyloid and other unspecified amino acid sequences in addition to the β amyloid sequence and the sequences encompassed by the GXXXG and GXXXGXXXGG motifs. Given that the broad range of peptides is claimed, it is apparent that the instant specification fails to disclose any species of antigenic peptides that comprise any fragments of β amyloid and unspecified amino acids or structural motifs set by GXXXG and GXXXGXXXGG other than SEQ ID NO:1-6. Thus, the failure of disclosure is not sufficiently representative of the broad genus of structurally different antigenic peptides other than β amyloid sequences of claim 25.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 19, 20 and 23-30 stand rejected under 35 U.S.C. 102(b) as being anticipated by Nicolau et al. (PNAS, 2002 vol. 99, no. 4, p. 2332-2337, IDS reference, of record) for the reasons set forth in the office action mailed on 3/24/10.

Nicolau et al. teach administration of antigenic composition comprising a peptide comprising the claimed SEQ ID NO:1 in a reconstituted liposome comprising phospholipids and cholesterol (Fig.1, p. 2333) in PBS (e.g. pharmaceutical carrier). Further, Nicolau et al. teach that a hydrophobic (e.g. palmitoylic acid) tail is attached to a lysine residue of the peptide (Introduction, p. 2332) and the peptide is derived from Aβ amyloid sequence.

Claims 28-30 are included in this rejection because the SEQ ID NO:1 has GXXXG and GXXXGXXXGG motifs as is evidenced by the specification of the instant application in p. 25-26.

Given that the identical antigenic composition is administered to a group of subject having Aβ plaques (p. 2333, col. 2), the referenced composition inherently enhances the antigenicity in a patient of Alzheimer's disease.

Even if the claimed method does not recite a particular patient population, the patient population having Aβ plaques cannot be excluded from the study because having Aβ plaques is considered as indication of Alzheimer's disease (p. 2332). Thus, prior art population and the potential population of the claimed method are considered identical. Therefore, the reference teachings anticipate the claimed invention.

Applicant's arguments filed on 8/18/10 have been fully considered but they were not persuasive.

Applicant has asserted that the Nicolau et al. is not a proper anticipatory reference as the reference fails to teach an increase in levels of memory restoration and curiosity awakening. Applicant has further asserted that the Nicolau et al. express serious doubt to the NOBRA mouse model in the treatment of Alzheimer's diseases because the NOBRA model does not provide a blood-brain barrier to cross for the antibodies to reach the pancreatic plaques. Applicant has traversed that the Nicolau et al. do not provide any evidence that the antigenic structures for clearing plaques from the brain based *in vitro* data of Fig 4.

Contrary to Applicant's assertion, the claimed method does not require specific method of clearing plaques from brain. The claimed invention recites "administering" of supramolecular construct regardless of the routes of administration. Given that the identical composition to the claimed invention is being administered to the same patient population, the administration of the composition will inherently achieve the intended purpose of the claimed invention - enhance antigenicity, increase memory restoration and curiosity awakening.

Applicant interprets that the Fig 4 of the Nicolau as lack of evidence for clearing plaques from the brain but antibodies to Aβ completely sequester plasma Aβ and all mechanisms involving antibodies are involved in clearing of the Aβ plaques (p. 2337, last 2 paragraphs).

Further, Nicolau et al. suggest different mechanisms of destruction of plaques including opsonization of the plaques and the subsequent destruction by microglia macrophages, alteration of the transport and equilibrium of β amyloid between brain and plasma and direct interaction of β amyloid antibodies with the plaque and all are involved in clearance of the Aβ plaques.

Note that Fig. 4 (p. 2335) has demonstrated disaggregation of β amyloid fibrils and this indicates the reduction of β amyloid plaques (abstract). Given that the Aβ plaques are cause of pathological conditions of AD, the removal of the Aβ suggests treatment for the diseases. Note that the results indicated that the palmitylated β amyloid peptide reconstituted in liposomes-lipid A are highly immunogenic, eliciting "therapeutic" antibody titers within 3 months of the first inoculation and preventing β amyloid plaque formation in young animals or significantly reducing existing plaques in older transgenic mice (abstract, Figs 2-5). Therefore, the reference teachings anticipate the claimed invention and the rejection is maintained.

11. The following new ground of rejection is necessitated by Applicant's amendment filed on 8/18/10.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 19, 20 and 23-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The specification or the original claims as filed does not provide a written description the phrase "and increased levels of memory restoration and curiosity awakening as compared to prior to administration". Applicants assert that the currently added limitation is found from the

specification in p. 23. However, the specification of the instant application discloses that the memory restoration and curiosity awakening are observed but there is no indication that the studies have been performed to compare the increase of such conditions.

The instant claims now recite a limitation which was not clearly disclosed in the specification as filed, and now changes the scope of instant disclosure as filed.

Such limitations recited in the present claims, which did not appear in the specification as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C.112.

14. No claims are allowable.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to YUNSOO KIM whose telephone number is (571)272-3176. The examiner can normally be reached on M-F,9-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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June 30, 2011

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